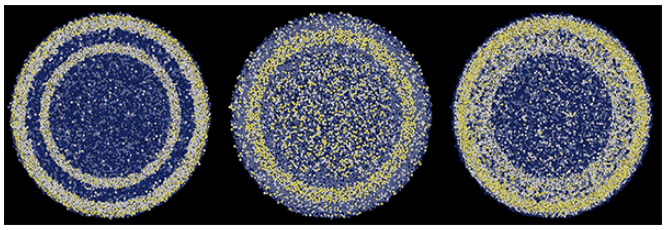
A new technology reveals the genetic origin of newborn neurons in the brain

3 March 2016



This is an expression of all the genes of a neuron during the first hours after its birth. Each circle represents a development stage (6h, 12h, 24h), and the colored points within each circle represent the level of gene expression. Credit: Jabaudon Lab, UNIGE

Our brain is home to different types of neurons, each with their own genetic signature that defines their function. These neurons are derived from progenitor cells, which are specialized stem cells that have the ability to divide to give rise to neurons. Today, neuroscientists from the Faculty of Medicine at the University of Geneva (UNIGE) shed light on the mechanisms that allow progenitors to generate neurons. By developing a novel technology called FlashTag that enables them to isolate and visualize neurons at the very moment they are born, they have deciphered the basic genetic code allowing the construction of a neuron. This discovery, which is published today in *Science*, allows not only to understand how our brain develops, but also how to use this code to reconstruct neurons from stem cells. Researchers will now be able to better understand the mechanisms underlying neurological diseases such as autism and schizophrenia.

Directed by Denis Jabaudon, a neuroscientist and neuroscientist at the Department of Basic Neurosciences at UNIGE Faculty of Medicine and neurologist at the University Hospitals Geneva (HUG), the researchers developed a technology termed FlashTag, which visualizes neurons as they are being born. Using this approach, at the very moment where a progenitor divides, it is tagged with a fluorescent marker that persists in its progeny. Scientists can then visualize and isolate newborn neurons in order to dynamically observe which genes are expressed in the first few hours of their existence. Over time, they can then study their evolution and changes in gene expression. &laquoPreviously, we only had a few photos to reconstruct the history of neurons, which left a lot of room for speculation. Thanks to FlashTag, there is now a full genetic movie unfolding before our eyes. Every instant becomes visible from the very beginning, which allows us to understand the developmental scenario at play, identify the main characters, their interactions and their incentives", notes Denis Jabaudon. Working in the cerebral cortex of the mouse, the scientists have thus identified the key genesto neuronal development, and demonstrated that their expression dynamics is essential for the brain to develop normally.

A very precise primordial choreography

This discovery, by giving access to the primordial code of the formation of neurons, helps us to understand how neurons function in the adult brain. And it appears that several of these original genes are also involved in neurodevelopmental and neurodegenerative diseases, which can occur many years later. This suggests that a predisposition may be present from the very first moments in the existence of neurons, and that environmental factors can then impact on how diseases may develop later on. By understanding the genetic choreography of neurons, the researchers can therefore observe how these genes behave from the start, and identify potential anomalies predicting diseases.

After successfully reading this genetic code, the scientists we able to rewrite it in newborn neurons. By altering the expression of certain genes, they were able to accelerate neuronal growth, thus

altering the developmental script. With FlashTag, it is now possible to isolate newborn neurons and recreate cerebral circuits in vitro, which enables scientists to test their function as well as to develop new treatments.

A website open to all

The UNIGE team posted a website where it is possible to enter the name of a gene and observe how it is expressed, and how it interacts with other genes. &laquoEach research team can only focus on a handful of genes at a time, while our genome is made up of close to 20,000 genes. We therefore made our tool available for other researchers to use it, in a fully open way," highlights Denis Jabaudon.

More information: "Sequential transcriptional waves direct the differentiation of newborn neurons in the mouse neocortex" *Science* (2016). DOI: 10.1126/science.aad8361

Provided by University of Geneva